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A Clinical Review of the Management of Deep Vein Thrombosis

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Abstract- Background: Deep vein thrombosis or DVT is a blood clot that forms within a deep vein typically in the lower leg or thigh, although they can also occur in other parts of the body. This thrombus/clot prevents the flow of blood in that vein leading to swelling and pain. When a part of the clot breaks off from the main thrombus it is known as an embolus. The most feared complication of DVT is pulmonary embolism, which is potentially life-threatening, in which the embolus travels to the lungs. Pulmonary embolism is thought to be one of the most common causes of preventable deaths in hospitals in the U.S. Other complications include post thrombotic syndrome which can affect up to 50% of patients who develop DVT. DVT is estimated to occur at an incidence of 1 per 1000 adults annually with an increased risk in males versus females and is most common in adults over the age of 60. Venous thromboembolism (VTE) is the term given to include both deep vein thrombosis as well as pulmonary embolism.

Aim: Provide an update on the proper management of DVT to reduce morbidity and mortality.

Methods: A review of online publications and medical journals.

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A CLINICAL REVIEW OF THE MANAGEMENT OF DEEP VEIN THROMBOSIS

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Niketh Desouza ^α & Mishal De Souza ^ο

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Aim: Provide an update on the proper management of DVT to reduce morbidity and mortality.

Methods: A review of online publications and medical journals.

Conclusion: The primary goal of treatment is to prevent the clot from enlarging, breaking off and causing a pulmonary embolism, preventing new clot formation and to prevent long-term complications such as post thrombotic syndrome. The mainstay of treatment is anticoagulation². Compression stockings should be worn to prevent the development of post thrombotic syndrome. Inferior vena cava filters can be used in patient where anticoagulation therapy is contraindicated. Other rarer forms of treatment include thrombolysis and thrombectomy.

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I. INTRODUCTION

Deep vein thrombosis is an underdiagnosed, serious but preventable medical condition. It can happen to anybody which is why it is important to know about. Risk factors for developing DVT are inherited blood clotting disorders such as Factor V Leiden thrombophilia, prolonged bed rest, immobility, injury, surgery, hormone replacement therapy, birth control pills, cancer, heart failure, inflammatory bowel disease, prior history of DVT/PE, family history of DVT and age over 60³. The classical symptoms of DVT are warmth, pain, redness and swelling of the affected limb. A clinical diagnosis of DVT can be done using Well's score which indicates the clinical probability of having a DVT. However radiologic studies should be done to

confirm or rule out the diagnosis such as lower extremity Doppler studies, contrast venography and MRI/CT scanning. D-Dimer testing can be done to rule out DVT if the clinical probability for having one is low⁴. Once the diagnosis is made treatment can be initiated via the following techniques which we will discuss in detail below.

II. ANTICOAGULATION

The most common treatment of DVT is by using anticoagulants. This is due to the fact that they are non-invasive, treats up to 90% of patients, has a low risk of complications and is shown to reduce morbidity and mortality. Initial anticoagulation (i.e. 5-10 days) can be done with the following medications⁵:

- Low molecular weight heparin (subcutaneous): enoxaparin, dalteparin and tinzaparin.
- Factor Xa inhibitor (subcutaneous): fondaparinux.
- Unfractionated heparin (intravenous).
- Direct factor Xa inhibitors (oral pill): rivaroxaban and apixaban.

All patients should be assessed before and during anticoagulation therapy for their bleeding risk. Certain factors such as weight loss, renal failure and pregnancy may affect the half-life of the anticoagulant. The appropriate agent can be selected based on clinician's experience, patient's risk of bleeding, cost, patient's comorbidities and preference. Certain patients can be treated on an outpatient basis based on their preference and clinical condition. They should be hemodynamically stable, have a low risk of bleeding, normal kidney functions and have a system in place for the surveillance and administrations of the therapy⁶. After the initial therapy, long term anticoagulation should be initiated for a finite period of usually three to six months and may also extend up to twelve months in certain scenarios. Usually direct factor Xa inhibitors (rivaroxaban, apixaban, edoxaban) are preferred because they can be taken orally and do not require monitoring. Warfarin can be used but required periodic checking of the patient's International normalised Ration (INR). Long-term anticoagulation can be either subcutaneous or oral. Patient's preferences are particularly important in selecting a long term agent for anticoagulation. Full anticoagulation should be maintained during the transition period as this period has the highest risk of recurrent thrombosis. Once

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anticoagulation has been initiated and the patient's acute symptoms have resolved the patient should be encouraged to ambulate as tolerated.

III. TREATMENT RECOMMENDATIONS

1. Distal leg DVT:
 - Severe symptoms: Anticoagulation therapy for 3 months regardless of whether DVT was caused by a risk factor (surgery, hospitalization etc.) or was unprovoked.
 - Asymptomatic or mildly symptomatic: If no risk factors for clot extension (cancer, positive D-dimer, inpatient status) are present anticoagulation is not needed. Serial Doppler ultrasound examinations should be done over the next two weeks. If clot extension is noted anticoagulation therapy is begun for 3 months duration. If no extension is noted anticoagulation therapy is not required and no further testing is warranted.
2. Proximal leg DVT:
 - Should be treated with anticoagulation as outpatient if possible.
 - If DVT caused by surgery or mild risk factors (immobility, hospitalization or estrogen therapy) anticoagulation should be continued for 3 months.
 - If DVT was unprovoked, long term anticoagulation can be initiated if bleeding risk is not very high with physician reevaluating the patient every year or so.
3. Asymptomatic or incidentally found DVT:
 - Leg or pelvic DVT: anticoagulation therapy for same duration as discussed above.
 - Abdominal DVT (portal, splenic or mesenteric vein): anticoagulation therapy not required.
4. Cancer associated DVT:
 - Long term treatment with anticoagulation preferred unless bleeding risk very high. If bleeding risk is high then treatment for 3 months should be done. Low molecular weight heparin is preferred over warfarin.
5. Arm DVT (Axillary or proximal veins)
 - Upper extremity DVT not associated with central venous catheter: 3 months of anticoagulation is recommended.
 - Upper extremity DVT associated with a central venous catheter: Catheter should be left in place if functional and anticoagulation therapy continued as long as catheter is in place. Once catheter is removed anticoagulation should be continued for 3 more months⁷.
6. If a permanent risk factor is present such as thrombophilia is present or the patient has had two

or more episodes of DVT some experts recommend continuing anticoagulation therapy indefinitely.

IV. COMPLICATIONS OF ANTICOAGULATION

1. *Bleeding*: Patients can bleed more easily when taking anticoagulants such as heparin or warfarin. Patients should be counselled on medication dosing, strict compliance and methods to reduce the risk of bleeding such as avoiding contact sports and taking care while using sharp objects. Bleeding may develop in areas such as the nose or gums, excessive menstrual bleeding and bleeding in the urine/stool. Patients should also be told to avoid NSAID's and aspirin as these can increase their risk of bleeding. For cases of clinically significant bleeding reversal agents exist primarily for warfarin and heparin.
2. *Heparin induced thrombocytopenia (HIT)*: This occurs in patients receiving various forms of heparin. The platelet count begins to decrease 5-14 days after the initiation of heparin therapy. The patient can be clinically asymptomatic. There can be an extension of the previous clot or the formation of a new clot somewhere else in the body. Patients receiving heparin intravenously may have systemic reaction with fevers, chills, tachycardia and chest pain. Diagnosis involves the findings of thrombocytopenia, platelet 4 antibodies and heparin induced antiplatelet antibodies. The treatment of HIT consists of stopping all heparin products and using a direct thrombin inhibitor such as argatroban or lepirudin.
3. *Warfarin induced skin necrosis*: This occurs due to acquired/innate protein C deficiency in patients taking warfarin. It occurs between the third and tenth day of warfarin therapy. Symptoms range from pain and redness in the affected area initially to the formation of large bullae with eventual necrosis and eschar formation. It occurs in areas with subcutaneous fat such as breast, buttocks and thighs. Treatment includes discontinuing warfarin while initiating heparin, fresh frozen plasma and subcutaneous vitamin K. Care of the necrotic wound should be done with appropriate antibiotics, wound care and surgical interventions where necessary.

V. THROMBOLYTICS

Thrombolytic agents such as streptokinase and urokinase contain an enzyme which helps in the lysis of the already formed clot which will lead to normalised blood flow through the previously obstructed vein. They are usually administered directly to the clot through a catheter directly into the affected vein under imaging guidance. Systemic administration can also be done but this is not preferred as it has more bleeding complications and is a less targeted approach.

Thrombolytics help lower the incidence of post thrombotic syndrome and pulmonary embolism. Thrombolytics are administered in patients who present with an acute proximal DVT, having symptoms of less than 14 days duration, have a low risk of bleeding, good functional status and a life expectancy of more than 1 year⁸. Anticoagulation is preferred however due to the lower incidence of bleeding complications. The only real indication for thrombolytics are patients with an acute PE who are unstable (hypotension [systolic BP <90]) or have right ventricular dysfunction.

VI. IVC FILTER

These are used to decrease the risk of pulmonary embolism in a patient with contraindications to anticoagulation therapy. They prevent blood clots from travelling to the heart and lungs. Some of the contraindications to anticoagulation therapy include intracranial bleeding within 3 months, active bleeding, coagulation defects, severe thrombocytopenia and malignant hypertension⁹. Some of the risk factors for anticoagulation associated haemorrhage are increasing age, alcoholism, liver disease and chronic corticosteroid use. IVC filter may also be placed if there are recurrent pulmonary embolisms despite the use of anticoagulation, prophylaxis before surgery in patients with DVT, poor compliance with anticoagulants and right ventricular dysfunction with and enlarged right ventricle on echocardiography. In the last indication the disease is so severe that an IVC is placed because the next PE, however small it maybe, could be fatal. IVC filters are either permanent or non-permanent. Non-permanent filters can be retrieved or repositioned up to a certain amount of time. The procedure is done under local anaesthesia and the filters are introduced through the jugular or femoral vein via fluoroscopy guided or ultrasound guided techniques. In the long term however IVC filters can increase the risk of thrombus formation.

VII. THROBECTOMY

Before the introduction of intravenous heparin, open surgical thrombectomy was the only means to effectively treat an acute symptomatic DVT. However there were many disadvantages of this approach. During the procedure there can be significant blood loss. Retrombosis also occurs in many patients due to the damage to the venous endothelium by the previous clot itself or mechanically during the surgery. Postoperatively the patient would also be at risk for various wound complications¹⁰. Hence thrombectomy has a very limited role in the present day treatment of DVT.

VIII. PREVENTION OF DVT

Inpatients: High risk patients undergoing certain surgeries such as bone or cancer surgeries can be

prescribed anticoagulants to reduce the risk of DVT. Patients should be encouraged to ambulate as tolerated when they can. Compression stockings are recommended for immobilised patients or those who have a contraindication to anticoagulation. Patients should be counselled and thought leg exercises to prevent DVT.

Prolonged travel: There is a two to fourfold increased risk of developing DVT during prolonged travel (longer than 6-8 hours). Patients should be explained methods to decrease DVT formation such as leg exercises, wearing loose fitting clothing, moving around every hour or so and avoidance of sedatives and alcohol which can impair the patient's ability to move around.

Pregnancy: Pregnancy induces a hypercoagulable state which increases the risk of VTE by about five times. Pregnant women with homozygous factor V leiden and a family history of VTE were advised to begin therapy with low molecular weight heparin and either continue with LMWH or a vitamin K antagonist for 6 weeks after delivery. Warfarin is not used in pregnant women as it is a known teratogen.

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